REMARKS

The Official action of July 18, 1996, has been carefully reviewed. Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

Claims 1 to 30 have been cancelled and re-written as new Claims 31 to 59 for convenience. The claims have been amended to correct minor informalities as follows: the terminology "wherein ... is/are as defined above" has been deleted as being redundant to the definition of the variable within the claim; the definition of "m" has been moved to its first occurence in a given claim; the missing article "and" has been inserted where required near the end of a listing of variables to conform with proper Markush practice; and the lettering of the variables for X in Claim 32 has been corrected to be in proper alphabetical order. Claim 55 has been drawn to a method of treating or preventing pain or nociception. Support for this amendment is found in the specification (e.g. on page 80, lines 18-20) and in the claims of the application as filed. The claims under consideration are Claims 31-59.

The title of the invention has been amended to read: MORPHOLINE COMPOUNDS ARE PRODRUGS USEFUL AS TACHYKININ RECEPTOR ANTAGONISTS. Applicants believe that this title is clearly indicative of the invention to which the claims are directed. The title describes the general class of compounds, indicates their general nature as prodrugs and describes their general utility. If the Examiner has any further suggestions regarding an appropriate title, Applicants would gratefully consider them.

As requested, the current status of the parent application has been noted in the specification.

The language in the claims "and, alternatively," has been changed to read "or" to avoid any potential for ambiguity in the claims.

Claims 1, 3, 5 to 10, and 20 to 30 stand rejected under 35 U.S.C. §112, second paragraph, for indefiniteness.

The Examiner was concerned that the expression "optionally joined together " in the definition of "Z" renders the claim indefinite by placing no definite limits or boundries on the claims.

Applicants drafted such language to cover compounds which possess a styrene group on the 2-position of the morpholine (i.e. morpholine-CH=CH-phenyl). Although the Applicants believe that the meaning of such terminology is clear from the specification, in the interest of compact prosecution in rewritting the claims as new Claims 31-59, the terminology has been modified to indicate that the double bond is "between the two carbon atoms". Applicants believe that such languge clearly indicates the optional presence of a double bond between the carbon atom of "Y" (if Y is -CHR^{15}-) and the carbon atom which bears "Z".

Accordingly, the rejection of Claims 1, 3, 5 to 10, and 20 to 30 under 35 U.S.C. §112, second paragraph, for indefiniteness has been overcome.

Claims 1 to 30 (now Claims 31-59) stand rejected under 35 U.S.C. §103 for obviousness over PCT Publication WO 94/00440.

The Examiner stated:

> The reference discloses for the same purpose as the claimed compounds which are close structural analogs of the claimed compounds as noted in the Examples. The claimed compounds are so closely related to the analogous compounds of the reference as to be structurally obvious therefrom in the absence of any unobvious properties especially since one of ordinary skill in the art would expect compounds so closely related structurally would have the same or essentially the same properties. The composition claims and method of use claims would likewise be obvious from the teachings of the reference absent a showing of unobvious or unexpected properties and/or results.

Applicants respectfully traverse this rejection and provide the following comments. As the Examiner will appreciate, the instant compounds are structurally disctinct from the compounds of PCT Publication WO 94/00440 (and related applications). Although the compounds disclosed in PCT Publication WO 94/00440 may be employed as starting materials for the claimed compounds, the claimed compounds are not close structural analogs of the compounds disclosed in the reference.

In particular, the claimed compounds possess a group "X" (i.e. on the heterocycle "B" or on a phenyl substituent) or a N-oxide on the nitrogen atom in the morpholine ring. The presence of the group "X" or the N-oxide clearly distinguishes and renders unobvious the claimed compounds with respect to the compounds in the cited reference. Compounds bearing one of the potential variables for "X" (i.e. "(a)" thru "(j)") or a N-oxide are certainly more complex than the corresponding unsubstituted compounds. The cited reference does not disclose or suggest such substitutents. The cited reference provides no motivation to introduce such substitutents. In addition, the cited reference does not indicate where on the molecule the substituents should be introduced, nor how compounds bearing such substiuents may be prepared.

Accordingly, the rejection of Claims 1 to 30 (now Claims 31-59) under 35 U.S.C. §103 for obviousness over PCT Publication WO 94/00440 is untenable and should be withdrawn.

Under 35 U.S.C. §121, the Examiner required restriction among: Claims 25 to 30, drawn to methods of treating or preventing different recited diseases. The Examiner required election of a single disclosed species for prosecution to which the claims shall be restricted if no generic claim is finally held to be allowable.

In response to such requirement, Applicants make the election to prosecute Claim 25 (now Claim 55) which is directed to a method for treating or preventing pain or nociception with the subject compounds, with traverse. However, Applicants respectfully request reconsideration and withdrawal of the requirement for restriction under 37 C.F.R. §1.143.

As stated in MPEP §803 there are two criteria for a proper requirement for restriction between patentably distinct inventions: (1) the inventions must be independent or distinct as claimed; and (2) there must be a serious burden on the Examiner if restriction is not required. As the Examiner noted, the species of disease are patentably distinct as claimed. Applicants respectfully assert, however, that there will not be a serious burden on the Examiner if restriction is not required.

Although the groups may be classified separately they may be searched without extra burden on the Examiner because they all share the instant compounds as a common element. The instant compounds provide an important material limitation to the claims which will facilitate examination. In addition, although they encompass divergent subject matter, they have not necessarily acquired a separate status in the art. As is recognized in the art, tachykinins may play a role in the etiology of the listed disorders/diseases and antagonism of tachykinin receptors may be useful in treating and preventing such disorders/diseases. Because no serious burden for examination is present if restriction is not required, Applicants respectfully request withdrawal of the requirement for restriction.

This election is being taken without prejudice to the filing of a divisional application directed to the non-elected subject matter. In accordance with the third sentence of 35 U.S.C. § 121, a patent issuing from the instant application should not be a reference against a divisional application filed before the issuance of such patent.

The Examiner believed that Claim 24 (now Claim 54) was generic. In this regard, Applicants note that this claim specifically focuses on the underlying biochemical ability of the instant compounds to antagonize the effect of substance P at its receptor site or to block neurokinin-1 receptors in a mammal. Although this method may certainly have implications in cerain disorders and diseases (including those disclosed in the specification), all that is required is that the designated biochemical effect be elicited.

Applicants gratefully acknowledge receipt and entry of the information disclosure statement sent December 6, 1995, and the supplemental information disclosure statement sent April 23, 1996. However, Applicants note that the first PTO-1449 form (pp. 1-4) initialed by the Examiner bears an incorrect serial number. Applicants graciously request that the Examiner initial the PTO-1449 form submitted with the IDS of December 6, 1995 (duplicate copy enclosed for the convenience of the Examiner).

Applicants respectfully contend that the application is allowable and a favorable response from the Examiner is earnestly solicited.

Respectfully submitted,

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Attachment: Duplicate copy of IDS sent December 6, 1995